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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,532	12/11/2003	Julian Edward Sale	18396/2002B	9057
29933	7590	01/18/2007	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199				SULLIVAN, DANIEL M
ART UNIT		PAPER NUMBER		
		1636		
MAIL DATE		DELIVERY MODE		
01/18/2007		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.	10/733,532	Applicant(s) SALE ET AL.
Examiner Daniel M. Sullivan	Art Unit 1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 December 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
- a) The period for reply expires _____ months from the mailing date of the final rejection.
 - b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) They raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) They raise the issue of new matter (see NOTE below);
 - (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. Applicant's reply has overcome the following rejection(s): _____.
6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1-12 and 14-16.

Claim(s) withdrawn from consideration: 17-31.

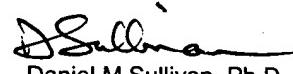
AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. Other: _____.


Daniel M Sullivan, Ph.D.
Primary Examiner
Art Unit: 1636

Continuation of 3. NOTE: The claims have been amended such that the method now requires that the rate of mutation in the cell be modulated by genetic manipulation of one or more DNA repair genes. As the previously examined claims were not limited to genetic manipulation of a subgenus comprising any DNA repair gene, entry of the amendment would necessitate reconsideration of the art of record and a new search to determine patentability of the claimed method under 35 USC §102 and 35 USC §103.

Continuation of 11. does NOT place the application in condition for allowance because:

Claim Rejections - 35 USC § 112

Claims 1-12 and 14-16 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing an immunoglobulin expressing cell line capable of directed constitutive hypermutation of target sequence wherein the rate of mutation in the cell is modulated by administering a mutagen or homozygous deletion of XRCC2 or XRCC3, does not reasonably provide enablement for the method wherein the rate of mutation is modulated by expression of any sequence modifying gene product or any gene deletion, conversion or insertion. This rejection is maintained for the reasons of record. Applicant's arguments for enablement of the claims are predicated upon entry of the claim amendments and are based, in part, on art that is not of record in the instant application (i.e., Cui X. et al. and Griffin, C.S. et al. cited in the paragraph bridging pages 11-12). As stated in the previous Office Action, although processes of gene deletion, conversion and insertion were known in the art at the time the application was filed, to the extent that the claims embrace targeted deletion, conversion and insertion, the skilled artisan would not know which genes to manipulate. In view

of the state of the art, which demonstrates that the effect of manipulating even closely related genes on mutation rate is unpredictable, the skilled artisan would not be able to practice the full scope of a method that broadly encompasses deletion, conversion or insertion of any gene without engaging in undue experimentation to identify which genes to manipulate and how (i.e., deletion, conversion or insertion) to manipulate them. Applicant's point that the claims do not require the rate of mutation be increased by the genetic manipulation is taken. However, the claims as they stand are generic to a wide variety of genetic manipulations and the skilled artisan cannot readily predict which of the genetic manipulations within the broad genus would result in any change at all in the rate of mutation. Whether or not the disclosure is enabling for a subgenus of genetic manipulation of one or more DNA repair genes would require further consideration, as the limitation was not presented prior to final rejection.

Double Patenting

Claims 1-12 **stand rejected** under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 36, 37, 39 and 40 of copending Application No. 10/146,505 (now U.S Patent No. 7,122,339) in view of Monteiro *et al.* (2000) *Teratogen. Carcinogen. Mutagen.* 20:357-386 for the reasons set forth in the previous Office Action (pp. 12-13). As stated in the previous Office Action, until such time as a terminal disclaimer is filed, the claims stand rejected. Note that, in view of the fact that the Application has now issued as a patent, this rejection is no longer provisional.

Claim Rejections - 35 USC § 102

Claims 1-12 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sale *et al.* (April 2000) WO 00/22111 (made of record in the IDS filed 11 December 2003) for the reasons of record. Applicant's arguments are predicated upon entry of the amendment. As the amendment has not been entered, these arguments are moot.